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CHRONICLE OF THE WORLD HEALTH ORGANIZATION

Malaria
Biological Standardization
Fellowship Programme
Visiting Lecturers

WORLD HEALTH ORGANIZATION
INTERIM COMMISSION

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CONTENTS

Page

Malaria :

First Meeting of the Expert Committee 101

Biological Standardization :

First Meeting of the Expert Committee 103

Adoption of International Standards :

Vitamin E 104

Heparin 105

Penicillin 105

Standardization of Antigenic Substances 107

Toxoids 107

Tuberculin 107

B.C.G. 109

Human Blood Antigens :

The A B O System. 110

The Rh System 110

Vitamins 110

Other Problems 111

Health Formalities :

Conference at Geneva of Experts on Passports and Frontier Formalities 111

Aid through Visiting Lecturers. 113

The Fellowship Programme of the Interim Commission 114

Ratifications of WHO Constitution 116

Representation of WHO at the Amazon Research Meeting 117

Publications :

Bulletin of the League of Nations Health Organization 117

Final Number of the *Bulletin of the Office International d'Hygiène Publique* 118

Epidemiological and Vital Statistics Report 120

Note by the Editor. — The *WHO Chronicle* is published at the end of each month in English, French and Spanish. Russian and Chinese editions are being prepared at the present time. The *Chronicle* is intended to summarize some of the activities of the Organization, without however claiming to be an authoritative record of the official views of the Interim Commission, wich are set out in the *Official Records of the WHO*. All correspondence relating to it should be addressed to the Geneva Office. Those who may wish to reproduce the text of this publication or extracts therefrom, more especially in the medical Press, are entirely at liberty to do so.

CHRONICLE OF
THE WORLD HEALTH
ORGANIZATION

VOL. I, No. 7-8 1947

MALARIA

First Meeting of the Expert Committee on Malaria held at Geneva in April 1947.

The world events of the period from 1939 to 1947 had far-reaching consequences for malaria, giving rise as they did not only to new problems, but also to new possibilities of combating the disease and even of eradicating it—a possibility hardly conceivable during the pre-war period. In the field of malaria the World Health Organization is now in a position to advance within measurable distance of its objective, " the attainment by all peoples of the highest possible level of health ".

Malaria remains a great obstacle to the attainment of this objective. One of the effects of the Second World War in many regions was to intensify morbidity and increase mortality due to malaria: during the war and post-war period there were serious malaria epidemics every year. UNRRA helped to meet emergency post-war needs,[1] but at the present time the only international organization in a position to furnish the necessary aid and technical co-operation is the World Health Organization. It should not be forgotten that malaria is still the most important among the diseases of tropical and subtropical regions, in both the East and the West, the prevention of which is feasible.

[1] In certain of the countries where it operated, especially in Greece, Yugoslavia and Italy, UNRRA furnished supplies and qualified personnel for the fight against malaria.

Broad perspectives have opened up for malariology, and it is no exaggeration to say that a new era has begun for the treatment of malaria and for methods of combating it.

The problem of malaria nevertheless remains so acute that the Interim Commission had good reason for its decision to appoint a Committee of Experts,[1] which held its first meeting at the Palais des Nations, Geneva, from 22 to 25 April 1947.[2] Its functions were to advise the Interim Commission concerning the creation and programme of a permanent Malaria Committee, with the help of the Draft Constitution submitted by Dr. GABALDON to the Interim Commission at its second session.[3] The Expert Committee, which is a temporary body, began its work with a detailed examination of Dr. Gabaldon's plan.

The Committee dealt both with use of chemotherapeutic substances and insecticides against malaria. During the course of the war, important progress was made in these fields. Methods of using the old drugs were perfected. To-day, new drugs and insecticides are largely employed.

As the war prevented to a considerable extent the dissemination of information on the experience gained in certain countries, the Committee felt that it would be useful for its report to include a summary of the present state of knowledge with regard to the fight against malaria.

The report [4] has two technical sections, one of which deals with anti-malarial drugs, and the other with the question of insecticides, especially DDT and the hopes and problems associated with it.

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[1] It will be recalled that the Malaria Committee of the League of Nations, composed of some fifty members, prosecuted wide and fruitful activities, especially in the field of epidemiology and in the treatment and combating of the disease. See " The Work of the Malaria Committee of the League of Nations since 1930 ", by Edmond Sergent (doc. C.H./Malaria/268).

[2] The Expert Committee comprised :

Dr. Mihai CIUCA, Roumania ;

Dr. N. Hamilton FAIRLEY, Great Britain ;

Dr. Arnaldo GABALDON, Venezuela (elected Chairman by the Committee) ;

Dr. Paul F. RUSSELL, United States of America ;

Secretary : Dr. Emilio J. PAMPANA, member of the Interim Commission Secretariat.

[3] See *WHO Chronicle* **1**, 3-4, p. 59.

[4] Doc. WHO.IC/79.

The section devoted to anti-malarial drugs, especially atebrin, sontochin and resochin (chloroquine and aralen), plasmoquine and pentaquine and, finally, paludrine, has a particular interest for the practising doctor. These technical sections of the report will probably be published in Volume I, No. 1, of the *World Health Organization Bulletin*.

BIOLOGICAL STANDARDIZATION

First Meeting of the Expert Committee at Geneva in June 1947.

Rational application of a therapy is possible only when medicaments of a known potency are used. This principle received early recognition from the League of Nations Health Organization, which set up a Permanent Commission on Biological Standardization. Before the Second World War, that body had fixed standards for thirty-five substances the titration of which can be effected only by biological methods, and had thus made a highly important contribution to the progress of therapeutics. The substances selected by the Permanent Commission for Standardization were made up, preserved and distributed by the Copenhagen and Hampstead (London) Institutes, and placed at the disposal of manufacturers and research workers in the various countries.

However, " a ' biological ' standard is obviously different from fixed standards, such as those for length or weight, in that it consists of a substance which is consumed in the course of its application. When a particular standard is nearing exhaustion and needs to be replaced, it is usually impracticable, and always unnecessary, to make a new standard preparation having exactly the same activity as the old one. What is required is that the value of the unit, as defined by an exact weight of the old standard, will not vary when re-defined in a weight of the new standard. The international unit, when once accepted, is thus permanent and unchangeable, though, in the course of many years, it is likely to be re-defined in terms of successive international standard preparations, and to be represented by a different weight of each. "[1]

Having regard to the necessity for replacing certain standards already consumed and of fixing others for substances not yet

[1] Dr. R. GAUTIER, *Bull. Health Org.*, 1945/46, **12**, 1.

standardized, the Interim Commission, on behalf of WHO—which is charged by its Constitution to continue the work in this field carried on by the League Health Organization—convened a Committee of Experts which met in Geneva from 9 to 13 June 1947.[1]

A summary of its work appears below.

Adoption of International Standards

The experts adopted international standards for vitamin E, heparin and penicillin, all widely used drugs in urgent need of international standardization.

Vitamin E.

This vitamin, present in certain foods, notably wheat-germ, is mainly used to combat sterility. An international standard for vitamin E would probably have been adopted at the Third International Conference on the Standardisation of Vitamins, planned to take place in the autumn of 1939, but as this conference could not be held because of the war, British members adopted in 1941 a provisional standard constituted by synthetic racemic α-tocopheryl acetate.[2] This standard was reviewed by the WHO group of experts and adopted as an international standard.

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[1] The Expert Committee comprised:

Professor E. Grasset, Director of the Health Institute, Geneva.

Dr. A. A. Miles, Director, Department of Biological Standards, National Institute for Medical Research, London.

Dr. J. Ørskov, Director, State Serum Institute, Copenhagen.

Lt.-Col. Sir Sahib Singh Sokhey, Director, Haffkine Institute, Bombay.

Dr. W. A. Timmerman, Director, National Institute of Public Health, Utrecht (elected Chairman by the Committee).

Dr. J. Trefouël, Director of the Pasteur Institute, Paris.

Dr. M. V. Veldee, Chief, Biologics Control Laboratory, United States Public Health Service.

Dr. Raymond Gautier, Counsellor of the Interim Commission *(Secretary)*.

[2] For a description of the standard preparation and what investigations led to its adoption, see *Bull. Hlth. Organ.*, 1941, 9, 436, 443, and *Nature*, Lond., 1941, 148, 472.

Heparin.

Heparin is a phosphatide present in various tissues but mainly in the liver, and used successfully as an anti-coagulant. On the initiative of the Department of Biological Standards of the National Institute for Medical Research, Hampstead, London, a provisional standard was established in 1942.[1] This was examined by the Committee of Experts and adopted as an international standard.

Penicillin.

Penicillin is one of the most powerful weapons in the modern therapeutic arsenal. This antibiotic produced by various strains of *Penicillium notatum* and *Penicillium chrysogenum* can now be obtained not only in great quantities but in highly purified forms.

There are four main types of penicillins : I, II, III and IV in the British notation or F, G, X and K in the corresponding American notation.

There is clear evidence that the several penicillins differ in their *in vitro* activity, both between themselves and in their action on different test organisms. The therapeutic efficacy of penicillins depends not only on their *in vitro* potency but on other factors such as absorption, excretion, and destruction in the body. Experimental evidence indicates that K is particularly discrepant in this respect, being inactivated much more rapidly than all other penicillins. American scientists have presented evidence that penicillins presumed to contain a large amount of K were relatively ineffective in the treatment of syphilis. The clinical efficacy of K is now questioned, though the evidence needs confirmation and cannot be regarded as established until clinical trials are made of pure specimens of the different penicillins.[2]

The possibility of establishing an international standard for penicillin, essential for its correct therapeutic application, was considered during the war by the Health Section of the League of Nations. A Conference convened in London in 1944, and attended

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[1] *Bull. Hlth. Organ.*, 1943, **10**, 144, 151.

[2] Note by the Department of Biological Standards, National Institute for Medical Research, Hampstead, London, doc. WHO.IC/BS/10.

by delegates of Australia, Canada, France, the United Kingdom and the United States of America, adopted two international standards : As master standard, a specimen of the pure crystalline sodium salt of penicillin II or G and as working standard a calcium salt of penicillin, the type of which was not specified.[1]

Since 1944, however, a change in the character of commercial penicillin has been observed in the United States, according to a joint statement of the Committee on Medical Research, the Public Health Service and the Food and Drug Administration.[2]

Previously, commercial penicillin was predominantly penicillin G or a mixture of G and F. Subsequently the G content showed a tendency to decrease, whilst the fractions F and K increased. This change is attributed to the use of various strains of *P. notatum* and *P. chrysogenum* and of different techniques for the growth of the mould and the purification of the final product. Some samples have contained a substantial proportion of penicillin K which is relatively inefficacious.[3]

Moreover, there have been reports that the different types of penicillin were unpredictable in their *in vitro* activity, and the opinion has been expressed that, in certain infections at least, *in vitro* activity may not be an adequate measure of *in vivo* activity. The question now arises whether or not the international standards agreed upon in 1944 are affected by the discrepancy between the *in vitro* and *in vivo* activity of the different types of penicillin.

It is possible that the sample of penicillin G used in the standards is, in the light of more refined methods of analysis, not as pure as was originally supposed.

In spite of this, the group of experts agreed that the standards set up in 1944 should for the time being remain. It was felt that, in the present state of our knowledge, it was not possible to define more precisely the existing standard, adopted as an international basis of comparison, until we have more knowledge of the properties of penicillins other than II or G.

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[1] For the report of this Conference and the results of the preliminary co-operative investigations, see *Bull. Hlth. Organ.*, 1946, **12**, 183.

[2] *J. Amer. Med. Assoc.*, 1946, 25 May, p. 271, see also " Commercial Penicillin ", by R. R. WILLCOX, *Brit. J. Vener. Dis.*, **23**, 1 March 1947.

[3] Since July 1946, many of the manufacturing difficulties were overcome. It was reported that practically all the commercial penicillin in the United States consisted predominantly of G.

Standardization of Antigenic Substances

The group of experts considered the possibilities of standardizing certain antigenic substances—namely, diphtheria and tetanus toxoids as well as tuberculin and BCG. In this field, they began pioneer work. Indeed, if it had been possible to standardize some antitoxins a long time ago by determining the necessary quantity of antitoxin to neutralize a known quantity of toxin, such a method could not have been applied to toxoids and vaccines. In the light of recent discoveries, however, it appeared to the experts that the time was ripe for an attempt to determine international standards for some of these widely used substances.

Toxoids.

It was pointed out that crystalline diphtheria and tetanus toxins had recently been produced by alcoholic fractionization, showing the possibility of establishing standards of high purity for toxoids.

The Committee, believing that the establishment of international standard preparations of diphtheria and tetanus toxoids was both possible and desirable, recommended that the specimens of highly purified toxoids offered by Dr. Veldee be submitted to the Department of Biological Standards, Copenhagen, and to certain laboratories in interested countries for examination, to ascertain their suitability as international reference preparations. The Expert Committee will reconsider these toxoids, when interested workers have expressed their views with regard to the desirability and possibility of adopting the preparations under study as international standards.

Tuberculin.

Tuberculin is a very complex substance obtained by the concentration of the media in which tubercle bacilli are grown. It is used for two main purposes :

(a) As a guide to the incidence of the tuberculous infection in a body which offers no demonstrable clinical reaction (Mantoux, von Pirquet and other skin tests) ;

(b) As a method of treatment for certain forms of tuberculosis.

From the time when tuberculin began to be employed it was obvious that the value of this new method of diagnosis depended

largely upon the exact knowledge of the potency of the preparation used.

Unfortunately, two batches of tuberculin may differ in potency even if prepared in exactly the same manner, by the same worker, in the same laboratory, with the same strain of tubercle bacilli, the same culture medium, and the same incubation time. The potency of tuberculin prepared in different laboratories using different strains of tubercle bacilli, culture media, etc., will often vary considerably. When the same dosage of such tuberculins with variable strength are used, almost any percentage of reactors can be obtained in the same population groups.[1] A comparison of the results of different tuberculin surveys is possible only when the same dose of tuberculin of the same strength has been used, or, within some limits, when the comparative strength of the tuberculin employed is known.

This was recognized by the Health Organization of the League of Nations, which in 1931 established an international standard constituted of Koch's " Alt-Tuberkulin " (Old Tuberculin).

When a new type of tuberculin, the " Purified Protein Derivative ", was developed by American workers, 500 times more active than O. T. when used in equal weight, and offering distinct advantages, especially in its application in the skin-tests, the question arose whether a new international standard was not urgently necessary. The Committee of Experts discussed this problem during the recent meeting, and recognized that there was a definite need for an international standard for P.P.D. It was decided that a preparation of P.P.D. originally obtained by Dr. Madsen and stored during the war at the National Institute of Health, Bethesda, should be transported from Washington to the State Serum Institute, Copenhagen, so that a comparative trial of this preparation by various workers could be made, with a view to its adoption as an international standard.

The Committee finally recommended that, when sufficient experimental data on the P.P.D. preparation are secured, interested workers should be invited to express their opinion upon the desirability and possibility of defining the biological activity both of P.P.D. and of Old Tuberculin in terms of international units.

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[1] From a note prepared by the State Serum Institute, Copenhagen, doc. WHO.IC/BS/16, 2 June 1947.

B.C.G.

B.C.G. is used for the prevention of prima tubercular infection in man. The method which has been used for more than 25 years is rapidly gaining in popularity. The number of persons treated with this vaccine is extremely high and there is no doubt that it will increase still more.

As the vaccine is a live preparation and cannot be preserved indefinitely, attempts have been made to ensure that the vaccinal suspension is always prepared under suitable conditions. Calmette felt the need of this, and he made it a rule in his laboratory that no B.C.G. strain should be issued abroad for human vaccination unless the Government of the nation applying for it appointed a laboratory to be officially entrusted with the task of preparing the vaccine under conditions guaranteeing perfect safety. Moreover, the personnel in charge of this work had to undergo a period of training at the Pasteur Institute, to familiarize themselves with the method of preserving the strain and of preparing the vaccine (Dr. BRETEY [1]).

In the opinion of Dr. J. ØRSKOV, member of the Expert Committee, it is impossible to achieve a real standardization of B.C.G. vaccine. Making a vaccine that will be uniform every time cannot be done, even when following explicit rules. This applies to B.C.G. as much as to any other live vaccine.

In his view, to arrange that the vaccine be made in the fewest possible number of laboratories, these laboratories maintaining close contact with one another and making mutual comparisons of their B.C.G. strains and vaccine, was more important than to establish standard rules now for the preparation of vaccine.

The Committee agreed that it was at present impracticable to set up a standard for B.C.G. vaccine, but, in order to meet the urgent need for uniformity of the B.C.G. vaccines in current use, the Committee recommended that :

(a) The original strain of B.C.G. kept at the Pasteur Institute, Paris, should be made internationally available ;

(b) The State Serum Institute, Copenhagen, which already distributes on behalf of the Committee a number of the

[1] Doc. WHO.IC/BS.27.

international preparations, should also distribute the B.C.G. strain ;

(c) The preparation and use of the vaccine in each country should be centrally co-ordinated.

Human Blood Antigens

The A B O System.

The Committee recommended that international standards for Anti-A serum and Anti-B serum should be established. To this end a pooled sample of high potency human Anti-A serum and one of Anti-B serum should be submitted to comparative tests by various workers and their potency expressed in appropriate units.

The Rh System.

The Committee recognized two urgent problems concerning the Rh antigens, namely :

(a) The provision of an agreed international nomenclature ;

(b) The establishment of standard antisera for those Rh antigens which are important in medical and obstetrical practice.

The Committee proposed to create an Expert Sub-Committee on Rh Antigens to study these two subjects and report on them. This Sub-Committee is to consist of geneticists and hæmatologists, to be proposed after consultation with interested workers in the various countries.

The Vitamins

It was considered that the following problems in the domain of vitamins were the most urgent :

(a) The replacement of the present international standard for vitamin A, which is a preparation of β carotene, by a standard consisting of a vitamin A ester.

The existing international preparation of β carotene should then be established as an international standard for β carotene, for agricultural purposes.

(b) The replacement of the existing international standards for vitamin D, which were respectively preparations of calciferol (vitamin D_2) and irradiated ergosterol, by an international standard consisting of vitamin D_3.

The experts proposed the creation of an Expert Sub-Committee on the Fat-soluble Vitamins to study these two subjects and report on them, the members of the Sub-Committee to include experts already at work on these problems.

They also discussed the vitamins not yet standardized, and considered that they were either sufficiently well characterized by physical and chemical means, or at this stage so ill-defined in their biological action as to preclude any attempt at standardization.

Other Problems

It was decided to replace the old international standard for Digitalis and Sulpharsphenamine, the stocks of both being almost exhausted. The experts also approved the emergency action taken by the National Institute for Medical Research, Hampstead, in replacing the standard preparations for several other substances, including Androsterone and Progesterone. The possibilities of setting up an international standard for Streptomycin were investigated, but it was generally agreed that the time was not yet ripe for such action.

* * *

It is clear that the task of the experts during this first meeting was very heavy. This was the result of the suspension of the activities of the Biological Standardization Commission of the League of Nations during the war and of the considerable progress achieved in medical science.

HEALTH FORMALITIES

Conference at Geneva of Experts on Passports and Frontier Formalities.

A meeting of experts of the Social and Economic Council of the United Nations was held at Geneva from 14 to 26 April 1947 for the purpose of formulating recommendations to serve as a basis for the next World Conference on questions relating to passports and frontier formalities to be held in November or December 1947. Dr. J. Fabre attended as observer for the World Health Organization.

Matters of interest to WHO related to health documents and health formalities at frontiers, viz. :

(1) Usefulness or otherwise of medical certificates such as are required by certain authorities of persons entering their territories ;

(2) The need to maintain or abolish the " Personal Declaration of Origin and Health " (recommended for adoption in Article 9 (4) of the International Sanitary Convention for Aerial Navigation, 1944) ;

(3) Certificates of inoculation and vaccination ;

(4) Health formalities at frontiers.

As regards (1) and (2), the Committee took no decision. As regards (3), the Committee urged Governments to accept, as evidence of vaccination and inoculation, certificates after the international health pattern as laid down by the International Sanitary Conventions now in force, with such modifications as WHO might subsequently wish to introduce. Certificates should be simplified, made uniform and reduced to the absolute minimum compatible with the safeguarding of public health.

As regards (4) the Committee agreed with the ICAO proposal : " The medical examination of crew and passengers with their baggage should be made without charge. The clothes and baggage of crew and passengers who have embarked in or passed through endemic areas should be subject to examination for disease vectors and insects. Such examination should be conducted as rapidly as possible by or under the supervision of the public health authorities.[1]

The Committee considered that all matters of interest to WHO should be submitted for opinion to the World Health Organization Expert Committee for the revision of the existing International Sanitary Conventions and thus permit suitable proposals in this connexion to be put forward at the First World Health Assembly.

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[1] This proposal refers chiefly to air travel.

AID THROUGH VISITING LECTURERS

A group of eight American and two Swiss medical experts has recently spent two months in a lecturing tour in Austria. The mission was organized by the Unitarian Service Committee of the United States of America and was the first travelling teaching unit to be sponsored by the World Health Organization Interim Commission.

The reasons for this visit have been explained by Dr. Brock CHISHOLM, Executive Secretary of the Interim Commission, in the following terms :

> " Thousands of doctors all over the world have lived behind the curtain of censorship during the war years, working alone and unable to share in the knowledge of their associates in other countries. Only a few will be able to travel to centres of new research. This is why top-ranking specialists in a dozen fields are volunteering for this two-month visitation to hospitals, clinics and universities. "

Throughout the tour, the members of the mission travelled as a group to the main centres of medical teaching (Vienna, Innsbruck, and Graz) lecturing, participating in conferences, and demonstrating new medical and surgical techniques and the use of some of the more recently developed sera and drugs.

Dr. Maurice B. VISSCHER, Professor of Physiology and Head of the Department of Physiology at the University of Minnesota, was Chairman of the Group and Dr. Erwin KOHN, Director of Medical Projects of the Unitarian Service Committee, acted as Executive Director. The mission also included Dr. John J. BITTNER, Professor of Cancer Research at the University of Minnesota ; Dr. McKeen CATTELL, Professor of Pharmacology at the Cornell University, New York ; Dr. Stuart C. CULLEN, Professor of Anæsthesiology at the University of Iowa ; Dr. Joseph P. EVANS, Associate Professor of Surgery at the University of Cincinnati, Ohio ; Dr. Chester M. JONES, Clinical Professor of Medicine at Harvard Medical School, Boston ; Dr. Eric MARTIN, Professor of Medicine at the University of Geneva ; Dr. Hermann MOOSER, Professor of Bacteriology and Hygiene at the University of Zurich, Switzerland ; Dr. S. Bernard WORTIS, Professor of Psychiatry at the New York University College of Medicine.

Some of the principal subjects of the lectures were lung and heart surgery, anæsthetics, surgical shock, frontal lobotomy and leucotomy, recent advances in cancer research, etc.

The results of this two months' visit have been highly gratifying. Austrian scientists and doctors were quick to appreciate the opportunity, the first since the war, to discuss important medical problems with their foreign colleagues, and to hear first-hand accounts of many of the recent developments in medical science and practice.

THE FELLOWSHIP PROGRAMME OF THE INTERIM COMMISSION

The international exchange of knowledge and experience is one of the principal factors in the solution of medical and health problems. Apart from international congresses, few organized attempts had been made up to the period of the First World War to promote this exchange. The knowledge, the experience and the technical information were confined to the individual countries.

The end of the first world war saw the recognition of the necessity for international action in the field of public health, and the Health Organisation of the League of Nations performed an invaluable function in promoting study tours and the exchange of personnel between the various countries. These international activities, carefully built up during the years of peace, ceased on the outbreak of the Second World War, apart from war-time contacts between the Western Allies. A large part of the European Continent, submerged beneath the German occupation, was cut off from the knowledge of recent developments in medical science.

This situation came to an end in the last stages of the war with the establishment of UNRRA, which regarded as one of its most important functions the supply of medical help, both in material and practical assistance, to countries devastated by the war. Among other activities in the programme of health rehabilitation, UNRRA made arrangements early in 1946 for thirty-five specialists to be sent as Fellows to the United States, Canada and some European countries.

After its creation, in July 1946, the Interim Commission of WHO took over from UNRRA the greater part of its health activities and considerably expanded its fellowship programme.[1] The names

[1] *WHO Chronicle*, 1947, 1, 3-4, 48.

of 172 men and women, specialists in public health and the basic medical sciences, as well as sanitary engineers, statisticians and nurses, from Austria, China, Czechoslovakia, Finland, Greece, Northern and Southern Korea, the Philippines, Poland and Yugoslavia, have been submitted to the Interim Commission for fellowships and travel grants up to the end of August, with a few score more to be expected from Hungary, Italy, Ukraine and Byelorussia.[1]

Plans have been made to send the Fellows to the United States, Canada, the United Kingdom, Sweden, Denmark, Switzerland, France, the Soviet Union, Netherlands, India, Egypt and even to exchange them between the aided countries in some special fields because, as is understandable, research and development in the medical sciences were not entirely extinguished even in war-stricken countries. In the host countries, the acceptance of fellows has been prepared in co-operation with the Universities, Governmental agencies, teaching foundations and by the personal visits of members of the staff of WHO to countries where the bulk of the Fellows are to be placed. Thus, for instance, in the United Kingdom a common effort was organized by the Ministry of Health, the British Post-graduate Medical Federation and the British Council to place and accommodate Fellows in such a way that their stay in England, already crowded with other students from the Dominions and Colonies, would be profitable. In the same way, some twenty-five Universities as well as other institutions were contacted in the United States and here, even though they are facing their own problem of war veterans returning to their medical studies, response was especially good.

On the Continent, owing to lack of time, only Sweden and Denmark were visited. In these countries most hearty co-operation was extended. Elsewhere contacts have been made generally through the country's representative on the Interim Commission of WHO whose effective help was much appreciated. Last but not least, Switzerland, the seat of the European Office, has absorbed a considerable number of Fellows in the best tradition of Swiss hospitality.

Financial responsibility for the programme rests entirely on the Interim Commission of WHO. Every Fellow—most of them University teachers or potential teachers, outstanding Public Health

[1] Of the 172 applications received up to 27 August, 64 have been favourably considered, 5 were refused, and 103 are still under consideration. Twenty Fellows were already in the field at that time.

men and specialists in all kind of medical techniques—will receive a reasonable monthly subsistence allowance, a special allowance for the purchase of technical books, tuition fees where necessary and travel expenses, including local travel in the country of study.

There is no doubt that the exchange of knowledge and experience in health is not only an immediate post-war measure but will continue so long as the promotion and protection of health is regarded as a paramount international concern.

Further development will depend largely on the return to normal international conditions. There is an urgent need to extend the programme of fellowships to all Member States of the World Health Organization. An endeavour should be made to concentrate on fewer Fellows for longer-term grants and to exercise extreme care in the selection of candidates. The programme should be approached not as an emergency measure but rather as an integral part of medical education.

RATIFICATION OF THE WORLD HEALTH ORGANIZATION CONSTITUTION : THE PRESENT POSITION

The Constitution of the World Health Organization, which was signed in New York in 1946 by 64 Governments, will come into force when 26 Member States of the United Nations have become parties to it. Six months at the latest after that date the World Health Assembly is to be convened.

Up to 15 September 1947, fifteen Member States of the United Nations had ratified or unconditionally accepted the Constitution : China, the United Kingdom, Canada, Iran, New Zealand, Syria, Liberia, Ethiopia, the Netherlands, Saudi Arabia, Turkey, Union of South Africa, Norway, Egypt and Sweden.

Seven States non-members of the United Nations have likewise ratified or unconditionally accepted the Constitution : Switzerland, Transjordan, Italy, Roumania, Albania, Eire and Austria.

REPRESENTATION OF WHO AT AMAZON RESEARCH MEETING

Dr. Fred L. SOPER, Director of the Pan American Sanitary Bureau, Washington, D.C., represented WHO at a meeting of the Scientific International Commission of the Hylean Amazon at Belem do Para, Brazil, on 12 August. The Commission is concerned with research activities into the flora and fauna of the tropical region of the Amazon basin as they affect the native population.

PUBLICATIONS

Bulletin of the League of Nations Health Organisation.

Number 3, Volume XII, of the *Bulletin of the League of Nations Health Organisation* was published, after the liquidation of the League, by the Secretariat of the Interim Commission of the World Health Organization, which fell heir to its functions.

Among the articles in this number, that on rabies is one of particular interest.

The International Rabies Conference of 1927 invited the Health Organisation " to publish statistics of the results of anti-rabies treatment in the different anti-rabies institutes of the world ". The object was to determine the conditions most favourable to the success of anti-rabies treatment and if possible to select from among the various methods of vaccination employed the one that offered the greatest measure of security.

Dr. A. G. MCKENDRICK was allotted the task of analysing the statistical data received. Up to 1937 he published nine successive reports dealing with 1,062,704 treated persons.[1] After his death in 1943, Major GREENWOOD, Professor Emeritus of Epidemiology and Vital Statistics in the University of London, was asked to complete the enquiry. The " Tenth Report on Data of Anti-Rabies Treatments supplied by the Pasteur Institutes ", which is the last of the series, makes a comprehensive survey of the results

[1] For previous reviews, see document L.o.N. C.H. 844 and the following *Health Organization Bulletins:* 1932, 1, 117 and 746; 1933, 2, 591; 1934, 3, 646; 1935, 4, 777; 1937, 6, 19; 1938, 7, 1; 1940, 9, 33.

obtained from a total of 1,670,848 treated persons. Here are the fruits of an experiment of unique scope in the history of anti-rabies treatment.

The first part of the article is devoted to the results of the Tenth Review, dealing with 228,051 persons treated since 1938. A series of tables shows the distribution of cases according to the vaccine employed, the species of biting animal, the severity and position of the bite, and the number of days elapsing between the bite and the commencement of treatment. Other tables give the respective percentages of treated persons who were bitten on the bare skin and through clothing, the number of cases of post-vaccinal paralysis, mortality by race of the victim and, finally, world mortality.

The second part of the article is devoted to a critical analysis of the views of the late Dr. Maria J. VAN STOCKUM, who had advanced the opinion that the classic Pasteurian treatment was valueless, and to a general discussion of the lessons to be learned from this important survey.

Other articles in this number include :

" The Biological Assay and Control of Tetanus Toxoid " (L. GREENBERG, J. GIBBARD and C. A. MORRELL) ; " On the Standardisation of Haffkine Institute Polyvalent Anti-snake-venom Serum against the Venoms of the Four Common Indian Snakes (Cobra, Common Krait, Russell's Viper and Saw-scaled Viper) " (A. K. HAZRA, D. C. LAHIRI and S. S. SOKHEY) ; " A Provisional Standard for Staphylococcus β Antitoxin " (Johs. IPSEN and O. ROSTOCK) ; " The Ecology of Sandflies at the Larval Stage and the Epidemiology of the Diseases transmitted by Them " (L. NÁJERA) ; " Nutrition in Rural Districts in Greece " (G. P. ALIVISATOS and Ad. JOUSTINIANOS).

Final Number of the
" Bulletin of the Office International d'Hygiène Publique ".

The October-November-December 1946 number of the *Bulletin* of the *Office International d'Hygiène Publique* was published under the joint auspices of the *Office* and the Interim Commission of the World Health Organization. This number will be the last of the series, as, in accordance with a mutual decision by the *Office* and the Interim Commission, the publication will be continued as the *Bulletin of the World Health Organization.*

This final number of the *Office Bulletin*, which mentions the Interim Commission of the World Health Organization on its cover, has a section devoted to the health laws and regulations of the Belgian Congo, the Principality of Monaco and Tunisia ; various analyses of medical works and articles ; health measures and information for the last quarter of 1946 ; and the communications and reports made to the Permanent Committee by delegates in the course of the October 1946 session, the chief of which are discussed below.

Of eight articles on tuberculosis, five deal with various aspects of the disease during the war : in England (Sir W. DALRYMPLE-CHAMPNEYS), Bulgaria (Dr. KOUSSITASSEF), Switzerland (Dr. P. VOLLENWEIDER), and France (Dr. LOTTE and Drs. AUJALEU, LOTTE & PÉQUIGNOT). Three others discuss the technique and results of anti-tuberculosis vaccination by means of BCG in France (Dr. LOTTE and Drs. L. NÈGRE & J. BRETEY) and Sweden (Dr. A. WALLGREN).

Smallpox is the subject of five other articles. One describes the importation of smallpox into England during the first half of 1946 and indicates the part played in the spread of smallpox cases by atypical forms of the disease which occur among subjects vaccinated a fairly long time ago (Dr. M. MACKENZIE). Two others discuss " immunity reaction " following vaccination against smallpox (Dr. J. C. BROOM and Dr. P. VOLLENWEIDER). The last two discuss the respective frequencies of post-vaccinal encephalitis in the Netherlands (Dr. C. VAN DEN BERG) and England (Dr. M. MACKENZIE) and lead to the conclusion that this complication could be avoided in most cases if children were vaccinated before the age of two.

Three articles are devoted to the cases of typhus fever which appeared at the end of the war in France (Dr. J. BOYER), England (Dr. M. MACKENZIE) and Portugal (Dr. A. CARVALHO DIAS).

Of two studies on plague, one points out the primary role played by rat-fleas in interhuman transmission of bubonic plague (Dr. N. H. SWELLENGREBEL), and the other emphasizes the good effects of the sulphanilamides, particularly sulphathiazole and sulphadiazine, in treatment (Dr. C. MANI).

Finally, there are a number of articles on a diversity of subjects such as the fight against typhoid fever in Warsaw during the second German occupation (Dr. LONTZKI), cerebro-spinal meningitis in French West Africa and in Togoland (Dr. PELTIER), persistent endemic foci of certain acute infectious conditions (Dr. W. CHODZKO), the propagation of venereal diseases in Bulgaria (Dr. KOUSSITASSEF),

the new organization of the Roumanian Academy of Medicine (Dr. DANIELOPOLU), epidemic poliomyelitis in Bulgaria from 1931 to 1945 (Dr. KOUSSITASSEF), malaria in Italy during the war (Dr. G. A. CANAPERIA), deratization of ships (Dr. P. G. STOCK), and control of anti-yellow-fever vaccine from the Pasteur Institute at Dakar (Dr. PELTIER).

Epidemiological and Vital Statistics Report.

The second number, July 1947, of the *Epidemiological and Vital Statistics Report*, the monthly supplement to the *Weekly Epidemiological Record*, gives detailed statistical information regarding the incidence of cholera, yellow fever, plague, typhus fever, smallpox and relapsing fevers.

The August issue, Vol. I, No. 3, contains an article on " Recent Birth-rate Trends " by Knud STOWMAN. The general impression, concludes the author, is that, while during the first third of the 20th century areas of low fertility were formed, which grew steadily larger and deeper, from the middle of the 1930's onwards, the tide began to turn and the birth rate rose in countries where they were lowest ; the Second World War did nothing to stop it. In Western and Northern Europe, in North America and Australia, the generation of women who were responsible for the fall of the birth rate is now reaching the end of its potentially fertile life. It is apparently being replaced by young women wanting and having more children. Meanwhile the birth rate continued to fall during another ten years in those countries in which the decrease in fertility occurred only at a later stage. Discussing future possible developments, the author points out that up to about 1960 a decreasing number of women will reach each year the age of the middle twenties—the best child-bearing age—on account of the low birth rates prevailing when they were born. Many of the men whom the young women of to-day expected to marry died in the war, and many young mothers became widows. The birth rate will therefore be struggling in the future against severe handicaps.

The number also contains statistical tables giving the birth rates in various countries, birth rates in the large towns of Europe and birth rates in some large towns in other parts of the world.

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